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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,494	06/27/2006	Gary P. Cook	02181.0087U2	9161

23859 7590 05/26/2010

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EXAMINER	
SHOMER, ISAAC	
ART UNIT	**PAPER NUMBER**
1612	

MAIL DATE	DELIVERY MODE
05/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,494	COOK, GARY P.	
	Examiner	Art Unit	
	ISAAC SHOMER	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-15,18,20-26,29,31,32,36-46,48 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-15,18,20-26,29,31,32,36-46,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *17 March 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 17 March 2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

The information disclosure statements filed 17 March 2010 fail to comply with 37 CFR 1.97(c) and as such will not be considered. This is because they lack:

1. Either the fee set forth in 37 CFR 1.17(p) OR

2. A Statement under 37 CFR 1.97(e).

See MPEP 609.04(b)(II). The examiner also notes that documents 5-15 and 28-33, which are not US prosecution documents, have not been provided in the file wrapper and would not be considered unless copies of these documents are provided, as required by 37 CFR 1.98(a)(2).

Claim Rejections - 35 USC § 112 1st Paragraph: New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 24, and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's newly added limitation requiring that the emulsifying agent is present at a concentration from about 0.1% to 10% in the aqueous phase is new matter not supported by the original disclosure or original claims. Applicant has support for the presence of the emulsifying agent from between 0% and 10%, as well as from 0.5% to 5% by weight, as of page 15 lines 9-11 of the specification. However, this does not lend support lower limit of "about 0.1%." See MPEP 2163.05(III) in regarding new matter and numerical range limitations.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-11, 13-15, 18, 20-26, 29, 31, 32, 36-46, 48, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vuaridel et al. (WO 2000/62761 A1) in view of Ozerov (US 2001/0035352), Plishka (US Patent 5,629,277) and Buwalda ("Molecular Aggregation in Water: The Interplay of Hydrophobic and Electrostatic

Interactions" University of Groningen, Doctoral Dissertation, 19 November 2001, specifically Chapter 5, pages 97-118).

The examiner has attached both Buwalda, Chapter 5, and Buwalda, Table of Contents, wherein the table of contents attests to the publication date of the dissertation.

Vuaridel et al. (hereafter referred to as Vuaridel) teaches a method of making microparticles comprising incorporating a biodegradable polymer in an organic phase, a water soluble substance in aqueous phase, homogenizing, removing the organic solvent, and isolating a microparticle, as of Vuaridel, abstract. As such, this appears to be an emulsion process. The water soluble substance may be the peptide triptorelin acetate and the biodegradable polymer may be poly(lactide-co-glycolide) (abbreviated as PLGA), as of Vuaridel, page 15 Example 1. PLGA is dissolved in the organic solvent ethyl acetate, and an aqueous phase is made combining triptorlein acetate and a surfactant such as Tween 80 Tween 80 (Polysorbate 80 or Polyoxyethylene (20) sorbitan monooleate) in water is made, as of Vuaridel, page 15 Example 1. The phases are homogenized, and microparticles with a mean size of 52 microns are isolated, as of Vuaridel, page 15 Example 1. Cosolvents, including benzyl alcohol, DMSO, DMF and others are suggested as of Vuaridel, page 8 lines 23-29. Oxytocin as a water soluble active substance to be encapsulated is suggested as of Vuaridel, page 12 line 23. Tweens are suggested as a suitable non-ionic surfactant (Vuaridel, page 10 lines 24-25), wherein the surfactant may be present from 0.01% to 50% by weight in the aqueous phase. Vuaridel further suggests the addition of salts to the aqueous phase to

adjust ionic strength and to create a zeta potential between the polymer particles, leading to particle repulsion, as of Vuaridel, page 11 lines 5-9.

Vuaridel does not teach the anion 1-hydroxy-2-naphthoate.

Ozerov (US 2001/0035352) teaches that particles with a higher zeta potential are better suspended in a bulk medium, wherein stable particles remain dispersed, whereas unstable particles for a precipitate, as of Ozerov, paragraph 0004.

Plishka teaches that 1-hydroxy-2-naphthoate is a known hydrotrope, as of Plishka, column 3 lines 2-7. Hydrotropes are compounds that increase the solubility of sparingly soluble solutes in the aqueous phase (and are distinct from surfactants, both structurally and functionally), as of Piskha, column 3 lines 9-16.

Buwalda, Chapter 5 (hereafter referred to as Buwalda) teaches that hydrotropes are known to act as solubilizing agents in drug formulations, as of Buwalda, page 99, last full paragraph. Buwalda teaches that relatively high concentrations of hydrotropes are needed to initiate solubilization, as compared with surfactants, as of Buwalda, page 100 last paragraph. Buwlada teaches ranges of hydrotropes from 0 M to 3.2 M, as of Buwalda, page 101, Figure 5.1.

It would have been prima facie obvious for one of ordinary skill in the art to have included 1-hydroxy-2-naphthoate (as of Plishka) into aqueous phase in the method of making the composition of Vuaridel. The skilled artisan would have been motivated to have done so because 1-hydroxy-2-naphthoate is a hydrotrope (as of Plishka) and as such would have predictably increased the particle repulsion, and thereby the dispersibility of the polymer microparticles (as of Ozerov) with a reasonable expectation

of success (as of Buwalda). This appears to be the effect desired by Vuaridel, page 11 lines 5-9, wherein the addition of salts to the aqueous phase to adjust ionic strength and to create a zeta potential between the polymer particles, leading to increased repulsion is suggested. The application of a known technique (addition of a hydrotrope to the aqueous phase) to a known product (the particle of Vuaridel) for improvement to achieve predictable results (greater solubility of the particles in water) is prima facie obvious. See MPEP 2143, Exemplary Rationale D.

While the surfactant concentration range of 0.01% to 50% by weight, as of Vuaridel, does not anticipate the instant claims, it does overlap. While the hydrotrope concentration range of 0 M to 3.2 M of Buwalda does not anticipate the instant claims, it does overlap. While the prior art does not disclose the exact claimed values, but does overlap: in such instances even a slight overlap in range establishes a *prima facie* case of obviousness. In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003).

Response to Arguments Regarding Unexpected Results

In applicant's arguments dated 17 March 2010 (hereafter referred to as applicant's arguments), applicant contends that placement of the organic ion in the aqueous phase, as opposed to the organic phase, unexpectedly allowed for greater loading of active agent, as of applicant's arguments, paragraph bridging pages 10 and 11. Applicant alleges that the experiments detailed in Table 6 (page 31) of the specification detail the claimed method of preparing particles, wherein the polymer and peptide were in the organic phase, whereas the organic ion was in the aqueous phase.

Applicant compares this to Tables 1-5 and Examples 1-2 of the specification, which are allegedly drawn to comparative data not claimed, as of applicant's arguments, page 11, top partial paragraph and first full paragraph. Applicant further contends that there are other unexpected advantages in regards to active release when the microparticle is made with the organic ion in the aqueous phase, as compared with a method wherein the organic ion is in the organic phase, as of page 11, first full paragraph of applicant's arguments.

To be of probative value, there must be a nexus between any secondary evidence and the claimed invention. See MPEP 716.01(b). In this case, there does not appear to be such a nexus. The examiner disagrees with applicant's assertion that the data presented on page 31 Table 6 represents the claimed method. Table 6 of the specification is drawn to encapsulation of a peptide in microparticles comprising the pamoate anion. This is unrelated to the instantly claimed invention because pamoate is not recited as the organic anion in any of instant claims 1, 18, and 36. As such, it does not naturally flow that any effect that could have been observed with the use of the pamoate anion in the making of a microparticle would have been observed in the presence of a different anion, and the data presented on page 31, Table 6 of the specification is not relevant to the instantly claimed invention. No data is presented as to why any effect that is observed for the pamoate anion would also be observed for other anions.

The examiner notes that a method, wherein sodium salts of the claimed anions were added to the aqueous phase in the method of forming a microparticle appears to

have been tested as of page 34, Table 8 of the specification. However, applicant has not provided any comparative test wherein the claimed method is compared to the closest prior art, or to a method that is more similar than that of the closest prior art. As such, applicant has failed to show any unexpected or superior results. Direct or indirect comparative tests are probative of non-obviousness, and applicant has failed to show comparative tests wherein processes with the claimed anions are compared with processes lacking the claimed anion. See MPEP 716.02(b)(III).

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ISAAC SHOMER whose telephone number is (571)270-7671. The examiner can normally be reached on 8:00 AM - 5:00 PM Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/I. S./
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612